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NING ZHANG

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Dahna S. Pasternak
ROBINS & PASTERNAK LLP
1731 Embarcadero Road Suite 230
Palo Alto, CA 94303

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FALK, ANNE MARIE

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UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte NING ZHANG and PAMELA R. CONTAG

Appeal 2007-1832
Application 09/464,795
Technology Center 1600

Decided: March 6, 2008

Before, DONALD E. ADAMS, TONI R. SCHEINER, and DEMETRA J. MILLS, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for lack of utility, written description and enablement. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

The following claim is representative.

38. A transgenic mouse comprising a panel of expression cassettes, said transgenic mouse produced by a method comprising the steps of

introducing a first expression cassette comprising a first promoter derived from a first stress-inducible gene into a mouse at an embryonic stage, said promoter operably linked to sequences encoding a first light generating polypeptide, and

introducing a second expression cassette comprising a second promoter derived from a second stress-inducible gene into said mouse at an embryonic stage, said promoter operably linked to sequences encoding a second light generating polypeptide and said second promoter derived from a different stress-inducible gene than said first promoter.

Cited References

S. Shibahara et al., "Structural organization of the human heme oxygenase gene and the function of its promoter," 179(3) *Eur. J. Biochem.*, 557-63 (1989).

Robert E. Hammer et al., "Spontaneous Inflammatory Disease in transgenic Rats Expressing HLA-B27 and Human β_2 M: An Animal Model of HLA-B27-Associated Human Disorders," 63 *Cell*, 1099-12 (1990).

John J. Mullinset al., "Transgenesis in Nonmurine Species," 22(4) *Hypertension*, 630-33 (1993).

Ann L. Boyd et al., "Review: Molecular Biology of Transgenic Animals," 71(Suppl. 3) *J. Anim Sci.*, 1-9 (1993).

Cungi Cui et al., "Reporter genes in transgenic mice," 3 *Transgenic Research*, 182-94 (1994).

Ewan R. Cameron, "Recent Advances in Transgenic Technology," 7 *Molecular Biotechnology*, 253-65 (1997).

Philip A. Wood, "Phenotype Assessment: Are you Missing Something?," 50(1) *Comp. Med.*, 12-15 (2000).

Grounds of Rejection

1. Claims 38, 40, 41, 45, 46, 49 and 65-68 stand rejected under 35 U.S.C. § 101, for lack of patentable utility.

2. Claims 38, 40, 41, 45, 46, 49 and 65-68 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement.

3. Claims 38, 40, 41, 45, 46, 49 and 65-68 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement.

DISCUSSION

Background

The invention relates to diagnostic mammalian models, test animals, and methods of use thereof for the identification and characterization of compounds. (Specification 1.)

The Specification indicates that, heretofore, no in vivo screening method has been described that allows screening of compounds in whole, live animals where real-time data could be collected concerning the effects of a test substance on, for example, specific aspects of toxicity and substance metabolism. (Specification 3.)

Claim Interpretation

The claims are directed to a transgenic mouse comprising a panel of expression cassettes. The transgenic mouse includes a first expression cassette comprising a first promoter derived from a first stress-inducible

gene into a mouse at an embryonic stage, said promoter operably linked to sequences encoding a first light generating polypeptide, and a second expression cassette comprising a second promoter derived from a second stress-inducible gene into said mouse at an embryonic stage, said promoter operably linked to sequences encoding a second light generating polypeptide and said second promoter derived from a different stress-inducible gene than said first promoter. The transgenic mouse claimed has no specific phenotype and therefore may have any phenotype provided by the incorporated expression cassettes.

1. Claims 38, 40, 41, 45, 46, 49 and 65-68 stand rejected under 35 U.S.C. § 101, for lack of patentable utility.

The Examiner argues that

a careful reading of the Specification reveals only one asserted utility for transgenic mice comprising multiple expression cassettes as recited in the claims. The asserted utility is to use the mice to identify agents that induce or repress expression of the reporter gene (i.e., the “light generating polypeptide”) with the express purpose of determining how various agents present in the environment affect native gene expression in humans and other animals and, more specifically, how the agents affect the particular genetic control elements present in the reporter constructs.

(Ans. 3.) The Examiner argues that the Specification fails to provide a utility that is generic to the entire scope of the claim. (Ans. 6.)

The Examiner bears the initial burden of showing that a claimed invention lacks patentable utility. *See In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995). (“Only after the PTO provides evidence showing that one

of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."). "When a properly claimed invention meets at least one stated objective utility under § 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958 (Fed. Cir. 1983).

The Examiner's argument is not that the Specification fails to disclose a utility for the claimed transgenic mouse, but that it fails to disclose a utility that is generic to the entire scope of the claim. (Ans. 6.) The Examiner argues that the asserted utility "is not applicable to the vast majority of transgenic mice covered by the claims." (Ans. 5.)

Appellants contend that "[t]he asserted utility is using live mice containing reporter constructs to monitor the effect of any molecule on the promoter." (Reply Br. 7.) Appellants assert there are "innumerable references establishing that reporter constructs containing a promoter derived from a selected gene operably linked to a reporter gene recapitulate gene expression such that the effect of a molecule on the gene (via the promoter) can be determined (see, page 3, lines 2-33 of the application; see also page 22, lines 2-12 of the application.)" (Reply Br. 7.)

We do not find the Examiner has presented sufficient evidence that the utility asserted by Appellants is unsupported. The Examiner, in fact, agrees that the asserted utility is applicable to some of the transgenic mice covered by the claims. Since the Examiner agrees that the subject matter claimed meets at least one stated objective utility, the rejection of the claims for lack of utility is reversed.

2. Claims 38, 40, 41, 45, 46, 49 and 65-68 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement.

The Examiner argues that

the specification provides the general methodology for making transgenic animals (see page 65, lines 2-7 and pages 65-68 of the specification), but does not describe any working example for producing a transgenic mouse as claimed and does not describe the expression characteristics of a transgenic mouse encompassed by the claimed invention. It is further noted that considering the fact that the art of making transgenic animals is highly unpredictable, the phenotypes and characteristics of the transgenic mice encompassed by the invention are not predictable.

(Ans. 8.)

However, as discussed herein, the claims do not require any specific phenotype for the claimed transgenic mouse. The claims require a transgenic mouse having first and second expression cassettes, each including a promoter derived from a stress inducible gene and a light generating polypeptide. Therefore the Examiner's reference to Cameron and Wood, and arguments concerning leaky expression in non-targeted tissues and unpredictable phenotype of the resulting mouse (Ans. 10) are not on point. The claims do not exclude leaky expression of the incorporated expression cassettes.

"The 'written description' requirement [under 35 U.S.C. § 112, first paragraph] implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to

satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). The written description requirement of 35 U.S.C. § 112, first paragraph, does not require a description of the complete structure of every species within a chemical genus. *See Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species the claim encompasses.) "[T]he written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002) (emphasis omitted, bracketed material original).

Appellants broadly claim a transgenic mouse containing two expression cassettes each including a promoter derived from a stress-inducible gene and a reporter polypeptide, such as luciferase. Appellants' Specification describes stress related genes and promoters known in the art at pages 22-23, 27 and 35-58. Reporter genes are described in the Specification, at pages 58-59. Methods of construction of the reporter expression cassettes are described in the Specification at pages 33-35. The Specification, pages 59-69, describes known methods of preparing

transgenic mice. Thus, Appellants have shown a complete disclosure of sufficiently detailed, relevant identifying characteristics of the claimed transgenic mouse, i.e., a complete or partial structure of expression cassettes including functional characteristics of reporter and promoter elements of stress inducible genes, that when coupled with a known or disclosed correlation between function and structure, describe the invention.

The Examiner argues that “due to the unpredictability of the site of integration of the transgene, when random integration methods are used, the final genetic context of the expression cassettes is not described.” (Ans. 8.) Appellants respond with the Declaration of David B. West, arguing that “routine at the time of filing were methods of assaying if a sequence from an expression cassette had been integrated into a host mouse’s genome and, if so, where such integration occurred. Such assay methods include, but are not limited to, PCR, Northern and/or Southern blotting (for example of particular tissues) as well as *in situ hybridization* and/or imaging techniques.” (Declaration of West ¶ 9.)

Since the mouse of the pending claims requires no specific phenotype or characteristic, we find the Examiner’s arguments concerning random integration and unpredictability of phenotype (Answer 10-11) to be inapplicable. We agree with Appellants that methods of assaying if a sequence from an expression cassette had been integrated into a host mouse’s genome are known, and methods of determining where such integration occurred are routine in the art. Thus we do not find the Examiner

has provided adequate reasoning why the Specification does not describe the technology that is sought to be patented.

The rejection of the claims for lack of written description is reversed.

3. Claims 38, 40, 41, 45, 46, 49 and 65-68 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement.

Although not explicitly stated in section 112, to be enabling, the Specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *In re Fisher*, 427 F.2d 833, 839 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. *In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971). An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993) (Examiner must provide

a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). *See also In re Morehouse*, 545 F.2d 162 (CCPA 1976). The threshold step in resolving this issue is to determine whether the Examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. Factors to be considered by the Examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*, 230 USPQ 546, 547 (BPAI 1986). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (footnote omitted). *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Examiner contends that due to the unpredictability in the transgenic art, the broad scope of the claims, the limited guidance of the specification, the lack of any working example and the quantity of experimentation needed to enable the instant claims across a very broad scope, undue experimentation would have been required for one skilled in the art to make and use the invention as claimed. (Ans. 22.)

We do not find the Examiner has met the burden of establishing a prima facie case of lack of enablement. Appellants broadly claim a transgenic mouse containing two expression cassettes each including a promoter derived from a stress-inducible gene and a reporter polypeptide, such as luciferase. Appellants' Specification describes stress related genes

and promoters known in the art at pages 22-23, 27 and 35-58. Again, reporter genes are described in the Specification at pages 58-59. Methods of construction of the reporter expression cassettes are described in the Specification at pages 33-35. The Specification pages 59-69 describes known methods of preparing transgenic mice. The claims do not require that the transgenic mice have a specific phenotype and thus the Examiner's reference to Hammer and Cui regarding the unpredictability of phenotype based upon the integration site of a single or multiple expression cassettes is not on point. The claims merely require that the expression cassettes be incorporated into the transgenic mouse. In view of the Specification's teachings, we do not find the Examiner has provided sufficient evidence to question enablement throughout the claim scope.

The enablement rejection is reversed.

SUMMARY

The rejections of the claims for lack of patentable utility, failing to comply with the written description requirement, and lack of enablement are reversed.

REVERSED

Ssc:

DAHNA S. PASTERNAK
ROBINS & PASTERNAK LLP
1731 EMBARCADERO ROAD SUITE 230
PALO ALTO, CA 94303